

U.S. Patent Application No. 09/628,186  
Amendment dated January 6, 2005  
Responsive to the office action of August 6, 2004  
Attorney Ref. No.: 037003-0280721  
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## II. REMARKS

### Preliminary Remarks:

Claims 1, 5, 10, 18, and 56-61 are currently amended and new claims 64-74 are added.

Claim 1 is amended to be directed to a method for radiolabeling a chelator-conjugated antibody or antibody fragment with a therapeutic radioisotope for administration to a patient, support for which is found in the specification; for example, at page 10, lines 20-22, and page 13, lines 23-25. Claims 56-59 are similarly amended to specify the radiolabeling of an antibody or antibody fragment.

Claim 1 is further amended to specify that the radiolabeled antibody or antibody fragment is produced having sufficient radioincorporation, sufficient immunoreactivity, and a specific activity of at least about 5 mCi/mg, such that the radiolabeled antibody or antibody fragment may be administered directly to the patient without further purification of the radiolabeled antibody or antibody fragment from unincorporated radioisotope. Production of a radiolabeled antibody or antibody fragment having sufficient radioincorporation for direct administration is described, for example, in the sentence bridging pages 10-11, and at page 11, lines 13-16. The substitution of the term "immunoreactivity" for "binding specificity" in claim 1, and also in claims 18, 60, and 61, is supported by the use of these terms synonymously and interchangeably in the specification; for example, see page 13, lines 25 and 28. Support for the production of a radiolabeled antibody or antibody by the claimed method that "may be administered directly to the patient without further purification of the radiolabeled antibody or antibody fragment from unincorporated radioisotope" is found in the specification, for example, at page 9, line 22, to page 10, line 2. As described in the specification, the words "further purification" in the description of the claimed invention refer to chromatographic and other separation techniques that are employed with the purpose of removing free or bound unconjugated radiolabel, and do not refer to preparatory steps such as filtration.

Claim 5 is amended to specify radioincorporation of greater than 95 %, support for which is found in the specification, for example, at page 17, lines 27-29, and page 28, lines 15-17, as well as in original claim 17 (now canceled).

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Claims 10, 56, and 57 are amended to depend on claim 1, in accord with their subject matter.

New claims 64-69 are directed to the disclosed radiolabeling method wherein the antibody is 2B8, as described in the disclosed examples (see pages 17-37). 2B8 is an antibody that is produced by hybridoma cells that were deposited with the American Type Culture Collection as ATTC deposit no. HB 11388 on June 22, 1993, under the provisions of the Budapest Treaty. Support for the deposit information is found in column 30 of U.S. Patent No. 6,682,734 (copy attached), which issued from U.S. Patent Application No. 08/475,813 that is cited on page 17, line 7, of the present application.

New claims 70-74 are directed to disclosed embodiments of the radiolabeling method. For example, radiolabeling to specific activity of over 10 mCi/mg, to a specific activity of at least 15 mCi/mg, or to a specific activity of about 20 mCi/mg, is described on page 7, line 25, at page 13, lines 14-16 and 29, and page 14, line 1. Performing the disclosed radiolabeling method at a temperature of from about 25°C to about 43°C is described on page 12, lines 15-19, and performing the radiolabeling method at pH 4.2 is described on page 12, line 24.

#### Patentability Remarks

##### 35 U.S.C. §102(b)

Claims 1-4, 6-8, 10-13, 18, 49, 52-55, and 60-63 were rejected under 35 U.S.C. § 102(b) as being anticipated by Alberts et al. (U.S. Patent No. 5,650,134), which describes radiolabeling chelator-linked somatostatin peptides with <sup>90</sup>Y to a specific activity of about 800 mCi/mg. The cited reference neither described nor suggested the presently claimed method for radiolabeling an antibody or antibody fragment with a therapeutic radioisotope such that the radiolabeled antibody or antibody fragment may be administered directly to a patient without further purification of the radiolabeled antibody or antibody fragment from unincorporated radioisotope. Withdrawal of the rejection is therefore respectfully requested.

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35 U.S.C. §112, Second Paragraph

Claims 1-16, 18, and 49-63 were rejected under 35 U.S.C. § 112, second paragraph, because the meaning of "sufficient binding specificity" is allegedly indefinite. The applicants respectfully traverse this ground of rejection. The claims are amended to be directed to a method for radiolabeling an antibody or antibody fragment. The specification clearly uses the term "binding specificity" to refer to the capacity of antibodies to bind specifically to their target antigen; *e.g.*, in describing the degradation of this capacity to bind specifically to antigen that occurs due to radiolysis of radiolabeled antibodies. For example, see page 13, lines 11-22. Persons of ordinary skill in the art would therefore clearly understand the meaning of "sufficient binding specificity" as it is used in claim 1 to describe radiolabeled antibodies or antibody fragments that are suitable for therapeutic administration. Withdrawal of the rejection for indefiniteness is respectfully requested.

The specification uses the terms "binding specificity" and "immunoreactivity" synonymously and interchangeably in describing the capacity of antibodies to bind specifically to their target antigen and the degradation of this capacity that occurs due to radiolysis. As the term "immunoreactivity" is more widely used in the published literature, the claims are amended by replacing the term "binding specificity" with the term "immunoreactivity." The amendment does not affect the scope of the claims and is not made for patentability purposes, since both terms are disclosed in the specification and are used in the specification with the same meaning.

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Conclusion

All objections and rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If any points remain in issue, which the Examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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